Scientific Abstract

A Phase I Study of Vaccination with Autologous, Lethally Irradiated Non-small Cell Lung Carcinoma Cells Engineered by Adenoviral Mediated Gene Transfer to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor

This clinical trial for patients with metastatic non-small cell lung carcinoma (NSCLC) will investigate the use as therapeutic vaccines of autologous, irradiated NSCLC cells engineered by adenoviral mediated gene transfer to secrete human granulocyte-macrophage colony stimulating factor (GM-CSF). A total of 25 patients will be treated at three different dose levels of vaccine. Each patient will receive inoculations of either $1x10^6$, $4x10^6$, or $1x10^7$ autologous NSCLC cells (secreting at least 40 ng of GM-CSF/10^6 cells/24 hours) subcutaneously and intradermally. Vaccinations will be given weekly times three and then every two weeks until the supply is exhausted.

The proposed study is based on pre-clinical experiments in murine tumor model systems which indicated that injection of irradiated tumor cells engineered to secrete murine granulocyte-macrophage colony stimulating factor generated potent, specific, and long lasting anti-tumor immunity. Efficacy of irradiated, GM-CSF expressing cells could be demonstrated in models of lung carcinoma, melanoma, renal cell carcinoma, colon carcinoma, bladder carcinoma, prostate carcinoma, sarcoma, neuroblastoma, glioma, leukemia, and lymphoma. A Phase I clinical trial of vaccination with autologous, lethally irradiated melanoma cells engineered by retroviral mediated gene transfer to secrete GM-CSF has confirmed these studies, demonstrating the consistent induction of potent anti-tumor immunity without significant toxicity. In this study, we will attempt to expand these principles to NSCLC. Because of the complexity and length of producing vaccines with retroviral vectors, the current investigation will examine the biologic activity of a greatly simplified method for vaccine preparation. In this trial, harvested tumor masses will be prepared to single cell suspension, infected overnight with an adenovirus expressing human GM-CSF, and then irradiated and frozen the following day.

The overall goals of the proposed phase I study are:

1. To determine the feasibility of preparing autologous, lethally irradiated, NSCLC cells engineered by adenoviral mediated gene transfer to secrete GM-CSF in patients with metastatic NSCLC.

2. To determine the safety and biologic activity of vaccination with autologous, lethally irradiated NSCLC cells engineered by adenoviral mediated gene transfer to secrete GM-CSF.

3. To evaluate the feasibility, safety and biologic activity of administering a second preparation of autologous, lethally irradiated NSCLC cells engineered by adenoviral mediated gene transfer to secrete GM-CSF.